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Examiner: Deepak R. Rao
Group Art Unit: 1624
Applicants: Jeremy Green et al.
For: INHIBITORS OF c-JUN N-TERMINAL KINASES (JNK) AND
OTHER PROTEIN KINASES

May 26, 2006
Cambridge, Massachusetts

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT REGARDING SEQUENCE LISTING

Sir:

Pursuant to 37 C.F.R. §1.821(f) and (g), I hereby state that the information recorded in computer readable form (CRF) is identical to the paper copy of the Sequence Listing and that the paper and CRF copies of the Sequence Listing do not include new matter.

Respectfully submitted,

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0.1 M HEPES buffer, pH 7.5, containing 10 mM MgCl₂, 2.5 mM phosphoenolpyruvate, 200 μM NADH, 150 μg/mL pyruvate kinase, 50 μg/mL lactate dehydrogenase, and 200 μM EGF receptor peptide. The EGF receptor peptide has the sequence KRELVEPLTPSGEAPNQALLR (SEQ ID NO: 3), and is a phosphoryl acceptor in the JNK3-catalyzed kinase reaction. The reaction was initiated by the addition of 10 μM ATP and the assay plate is inserted into the spectrophotometer's assay plate compartment that was maintained at 30°C. The decrease of absorbance at 340 nm was monitored as a function of time. The rate data as a function of inhibitor concentration was fitted to competitive inhibition kinetic model to determine the K_i.

For selected compounds of this invention, activity in the JNK inhibition assay is shown in Table 8. Compounds having a K_i less than 0.1 micromolar (μM) are rated "A", compounds having a K_i between 0.1 and 1 μM are rated "B" and compounds having a K_i greater than 1 μM are rated "C".

Table 8. Activity in the JNK3 Inhibition Assay.

No.	Activity	No.	Activity	No.	Activity
IIA-1	A	IIA-2	-	IIA-3	A
IIA-4	-	IIA-5	A	IIA-6	A
IIA-7	A	IIA-8	A/B	IIA-9	B
IIA-10	B	IIA-11	A	IIA-12	B/C
IIA-13	C	IIA-14	B	IIA-15	B
IIA-16	-	IIA-17	-	IIA-18	-
IIA-19	-	IIA-20	-	IIA-21	-
IIA-22	-	IIA-23	-	IIA-24	-
IIA-25	-	IIA-26	-	IIA-27	-
IIA-28	-	IIA-29	-	IIA-30	-
IIA-31	-	IIA-32	A	IIA-33	A
IIA-34	A	IIA-35	A	IIA-36	A
IIA-37	A	IIA-38	A	IIA-39	A